REMARKS

Further and favorable reconsideration is respectfully requested in view of the foregoing amendments and following remarks.

Status of Claims

As indicated on the Office Action summary page, claims 1-34 are pending in the application, and claims 1-11, 19 and 23-33 have been withdrawn. Applicants note that the Examiner indicates that claims 12-18 and 20-22 are rejected. Claim 34 is not indicated as rejected in this summary of the claims, however, it is rejected in the body of the Office Action.

Claim Amendments

Claim 12 has been amended to recite a method of promoting HGF production and suppressing anti-blood coagulation activity and LPL releasing activity of heparin fragment. Support for this amendment is found on page 7, lines 6-11 and page 27, lines 8-15 of Applicants' specification. The other claims have been amended in order to be consistent with this change.

Further, claim 12 has been amended to recite "administering to a mammal an effective amount of an oligosaccharide selected from the group consisting of a disaccharide . . . and tri- to hexasaccharides". Support for this amendment is found on page 7, line 15, and page 36, line 15 of Applicants' specification, as well as Figure 8 and the original claims.

Claim 13 has been amended to require that at least one of the groups be sulfated, in response to the Examiner's objection to the claim.

Claim 15 has been cancelled, without prejudice.

Claim 18 has been amended under the definition of formula (I) to recite "n is 0 to 2", and under the definition of formulas (V), (VI), (VII), and (VIII) to recite "m represents 1 or 1", in order to be consistent with amended claim 12.

Claim 34 has been amended to recite that R^3 represents carboxyl group and R^4 represents hydrogen. Accordingly, claim 34 is now consistent with claims 7 and 18.

Minor changes have also been made to the claims, in order to better comply with U.S. practice.

No new matter has been added to the claims by the above-discussed amendments.

Claim Objections

The objection to claim 13 as being of improper dependent form has been rendered moot by the above-discussed claim amendments.

Rejection of Claims Under 35 U.S.C. § 112, First Paragraph

The rejection of claim 34 under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement has been rendered moot by the above-discussed claim amendments.

Patentability Arguments

The patentability of the present invention over the disclosures of the references relied upon by the Examiner in rejecting the claims will be apparent upon consideration of the following remarks.

Rejection Under 35 U.S.C. § 102(b)

The rejection of claims 12-18 and 20-22 under 35 U.S.C. § 102(b) as being anticipated by Cahalon et al. (U.S. 2003/0130230) as evidenced by Seidel et al. (British Journal of Haematology) is respectfully traversed.

The Position of the Examiner

The Examiner takes the position that Cahalon et al. disclose a method for treating symptoms associated with the development and metastasis of malignancies comprising administering a heparin-derived saccharide compound. The Examiner also states that Cahalon et

al. disclose the administration of the compound to a mammal, a mouse. The Examiner asserts that the reference discloses the use of Applicants' elected species, and that Cahalon et al. disclose the heparin-derived saccharide compound exhibits a regulator effect that includes both up regulation and down regulation of cytokine activity, and may elicit the secretion of active cytokine. The Examiner states that Seidel et al. evidence that it is known that soluble heparin molecules include an increase in the cytokine hepatocyte growth factor. Thus, the Examiner asserts that it is apparent from what is disclosed that one practicing the method disclosed by Cahalon et al. would inherently be practicing the instantly claimed method of promoting HGF production.

Applicants' Arguments

Applicants respectfully disagree with the Examiner's position for the following reasons.

Applicants' amended claim 12 recites a method of promoting HGF production and suppressing anti-blood coagulation activity and LPL releasing activity of heparin fragment, wherein a heparin fragment having di- or tri- to hexa-saccharide structure is administered to a mammal.

Applicants' invention was completed based upon the following findings:

With the increase in the size of heparin fragment, HGF producing activity increases. On the other hand, anti-blood coagulation activity and LPL releasing activity decrease with the decrease in the size of heparin fragment.

As is shown in the enclosed Rule 1.132 Declaration of Mr. Kazuhiro Fukuta (one of the inventors of the present application), the minimum heparin fragment which has an ability of promoting HGF production is a disaccharide fragment, and the maximum heparin fragment whose anti-blood coagulation activity and LPL releasing activity are suppressed is hexa-saccharide fragment.

Therefore, a heparin fragment having di- to hexa-saccharide structure promotes HGF production without producing side effects, such as bleeding or arrhythmia caused by LPL.

The Examiner states that one practicing the method disclosed by Cahalon et al. would inherently be practicing the instantly claimed method of promoting HGF production, since Seidel et al. teach that soluble heparin molecules induce an increase in HGF.

However, Cahalon et al. merely disclose that heparin or heparin-sulfate derived saccharide compound is used for the treatment of cancer and that oligosaccharides having 2-10 sugar units inhibit tumor cell migration. Cahalon et al. neither teach nor suggest that a heparin di- to hexa-saccharide fragment (as recited in Applicants' claims) promotes HGF production and suppresses anti-blood coagulation activity and LPL releasing activity caused by a larger size heparin fragment.

In addition, the heparin fragments taught by Cahalon et al. undergo oxidation with periodic acid and subsequent reduction. (Please see paragraph 0016 of the reference, which is mentioned in lines 8-11 on page 5 of the Office Action.) On the other hand, the heparin fragment of the present invention does not undergo oxidation with periodic acid or reduction. Therefore, the structure of the heparin fragment of Cahalon et al. is distinct from that of the heparin fragment of the present invention.

Furthermore, Seidel et al. disclose that a low molecular weight heparin which is intravenously administered to a patient increases serum HGF. The low molecular weight heparin taught by Seidel et al. is Fragmin®, manufactured by Pharmacia-Upjohn (Table I). Fragmin® is a mixture of heparin 8-40 saccharide fragments. Thus, Seidel et al. merely teach that heparin 8-40 saccharide fragments have an ability to increase serum HGF. In addition, Fragmin® is used as an anticoagulant.

Thus, Seidel et al. neither teach nor suggest that a heparin di- to hexa-saccharide fragment promotes HGF production and suppresses anti-blood coagulation activity and LPL releasing activity caused by a larger size heparin fragment, as recited in Applicants' amended claims.

For these reasons, the invention of Applicants' claims is clearly patentable over the cited references.

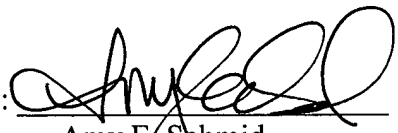
Conclusion

Therefore, in view of the foregoing amendments and remarks, it is submitted that each of the grounds of objection and rejection set forth by the Examiner has been overcome, and that the application is in condition for allowance. Such allowance is solicited.

If, after reviewing this Amendment, the Examiner feels there are any issues remaining which must be resolved before the application can be passed to issue, the Examiner is respectfully requested to contact the undersigned by telephone in order to resolve such issues.

Respectfully submitted,

Toshikazu NAKAMURA et al.

By: 

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